CONTENTS

PERSPECTIVE


SHORT COMMUNICATION


ARTICLES

Esterase Inhibition Attribute of Grapefruit Juice Leading to a New Drug Interaction. Ping Li, Patrick S. Callyer, Liang-Shang Gan, and Suresh K. Balani .................. 1023

Valproic Acid Induces CYP3A4 and MDR1 Gene Expression by Activation of Constitutive Androstane Receptor and Pregnane X Receptor Pathways. Lukas Cerveny, Lucie Svecova, Eva Anzenbacherova, Radim Vrzel, Frantisek Staud, Zdenek Dvorak, Jitka Ulrichova, Pavel Anzenbacher, and Petr Pavek .................. 1032

Biotransformation of 6-Methoxy-3-(3′,4′,5′-trimethoxy-benzoyl)-1H-indole (BPROL075), a Novel Antimicrotubule Agent, by Mouse, Rat, Dog, and Human Liver Microsomes. Hsien-Tsung Yao, Yu-Shan Wu, Yi-Wei Chang, Hsing-Pang Hsieh, Wei-Cheng Chen, Shih-Jung Lan, Chiung-Tong Chen, Yu-Sheng Chao, Ling Chang, Hsu-Yi Sun, and Teng-Kuang Yeh .................. 1042

5 Possible Bioactivation Pathways of Lamotrigine. Wei Lu and Jack P. Uetrecht ................ 1050

5 Effect of Perinatal Low Protein Diets on the Ontogeny of Select Hepatic Cytochrome P450 Enzymes and Cytochrome P450 Reductase in the Rat. Ganesh Cherala, Bernard H. Shapiro, and Anil P. D’mello .................. 1057


Metabolism, Pharmacokinetics, and Excretion of a Nonpeptidic Substance P Receptor Antagonist, Ezlopitant, in Normal Healthy Male Volunteers: Characterization of Polar Metabolites by Chemical Derivatization with Dansyl Chloride. Chandra Prakash, John O’Donnell, and S. Cyrus Khojasteh-Bakht .................. 1071

Identification of a Novel Glutathione Conjugate of Flutamide in Incubations with Human Liver Microsomes. Ping Kang, Deepak Dalvie, Evan Smith, Sue Zhou, and Alan Deese .................. 1081

Intestinal First-Pass Metabolism via Carboxylesterase in Rat Jejunum and Ileum. Kenji Masaki, Mitsuji Hashimoto, and Teruko Imai .................. 1089

Continued on next page

Selective Tissue Distribution of Tibolone Metabolites in Mature Ovariectomized Female Cynomolgus Monkeys after Multiple Doses of Tibolone. H. A. M. Verheul, M. L. P. van Iersel, L. P. C. Delbressine, and H. J. Kloosterboer 1105

Pharmacokinetic Parameters of Tibolone and Metabolites in Plasma, Urine, Feces, and Bile from Ovariectomized Cynomolgus Monkeys after a Single Dose or Multiple Doses of Tibolone. H. A. M. Verheul, C. J. Timmer, M. L. P. S. van Iersel, L. P. C. Delbressine, and H. J. Kloosterboer 1112

Application of the Dispersion Model to Describe Disposition Kinetics of Markers in the Dual Perfused Rat Liver. Selma Sahin and Malcolm Rowland 1119

Cytochrome P450 Eicosanoids are Activators of Peroxisome Proliferator-Activated Receptor α. Valerie Y. Ng, Yong Huang, L. Manmohan Reddy, John R. Falck, Emil T. Lin, and Deanna L. Kroetz 1126

Timolol Metabolism in Human Liver Microsomes Is Mediated Principally by CYP2D6. Marjo Volontinen, Miia Turpeinen, Ari Tolonen, Jouko Uusitalo, Jakka Mäenpää, and Olavi Pelkonen 1135

Improvement of the Oral Drug Absorption of Topotecan through the Inhibition of Intestinal Xenobiotic Efflux Transporter, Breast Cancer Resistance Protein, by Excipients. Tetsuo Yamagata, Hiroyuki Kusuhara, Mariko Morishita, Kozo Takayama, Hassan Benezet, and Yuichi Sugiyama 1142

The Prokinetic Cinitapride Has No Clinically Relevant Pharmacokinetic Interaction and Effect on QT during Co-administration with Ketoconazole. Marta Robert, Miguel Salvà, Rosa Segarra, Marco Pavesi, Ramón Esbrí, David Roberts, and Georg Golor 1149

In Vitro Metabolic Characterization, Phenotyping, and Kinetic Studies of 9cUAB30, a Retinoid X Receptor-Specific Retinoid. Gregory S. Gorman, Lori Coward, Corenna Kerstner-Wood, Lea Cork, Izet M. Kapetanovic, Wayne J. Brouillette, and Donald D. Muccio 1157

Abcg2/Bcrp1 Mediates the Polarized Transport of Antiretroviral Nucleosides Abacavir and Zidovudine. Guoyu Pan, Nagdeep Giri, and William F. Elmquist 1165

CYP2C9 Protein Interactions with Cytochrome b5: Effects on the Coupling of Catalysis. Charles W. Locuston, Larry C. Wienkers, Jeffrey P. Jones, and Timothy S. Tracy 1174

Predominant Contribution of UDP-Glucuronosyltransferase 2B7 in the Glucuronidation of Raceemic Flurbiprofen in the Human Liver. Yuji Mano, Takashi Usui, and Hidetaka Kamimura 1182

Metabolism and Disposition of a Selective α2 Nicotinic Acetylcholine Receptor Agonist in Humans. Christopher L. Shaffer, Mythul Gunduz, Renato J. Scialis, and Annie F. Fang 1188


Esterase Inhibition by Grapefruit Juice Flavonoids Leading to a New Drug Interaction. Ping Li, Patrick S. Callery, Liang-Shang Gan, and Suresh K. Balani 1203

Impact of Genetic Knockout of PEPT2 on Cefadroxil Pharmacokinetics, Renal Tubular Reabsorption, and Brain Penetration in Mice. Hong Shen, Scott M. Ocheltree, Yongjun Hu, Richard F. Keep, and David E. Smith 1209

Selective Toxicity of Aristolochic Acids I and II. Shinya Shibutani, Huan Dong, Naomi Suzuki, Shiro Ueda, Frederick Miller, and Arthur P. Grollman 1217


Isolation and Characterization of Polyspecific Mouse Organic Solute Carrier Protein 1 (mOscp1). Yasuna Kobayashi, Ayumi Tsu-chiya, Tomofumi Hayashi, Noriko Kohyama, Masayuki Ohbayashi, and Toshinori Yamamoto ............................... 1239

ERRATUM
Correction to “Three-Dimensional Quantitative Structure-Activity Relationship Analysis of Human CYP51 Inhibitors”. S. Ekins, D. C. Mankowski, D. J. Hoover, M. P. Lawton, J. L. Treadway, and H. J. Harwood, Jr. .. 1246


About the cover: A diagram showing the relationship between % remaining and the therapeutic blood or plasma concentration of 171 marketed compounds in which in vivo DDI information was incorporated. See the article by Watanabe et al. in this issue on page 1232.